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| 10/531,867 | 09/16/2005 | Tanya Kathleen Church | 270851US0PCT | 5987 |

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| EXAMINER | |
|---|---|
| ALSTRUM ACEVEDO, JAMES HENRY | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1616 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 03/04/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/531,867 | CHURCH ET AL. | |
| | Examiner | Art Unit | |
| | JAMES H. ALSTRUM ACEVEDO | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 12-22* is/are pending in the application.

4a) Of the above claim(s) *18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1-9 and 12-22 are pending**. Claims 18-22 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-3, 8-9, 12-13, and 16-17 have been amended. Claims 10-11 were previously cancelled. **Claims 1-9 and 12-17 are under consideration** in the instant office action. Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on November 11, 2009 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments. The previous rejection under §103(a) have been withdrawn per Applicants' amendments to describe the overall composition with "consisting of" claim language.

### *Election/Restrictions*

Claims 18-22 **remain withdrawn** from consideration by original presentation as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 1-9 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter).** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In Applicants' April 30, 2009 claim set the recitation of the propellant system as "consisting of…" was amended to "comprising of…" and support for this amendment was indicated to be found in original claim 1. Upon further consideration, this amendment is considered to introduce new matter, because original claim 1 only provides support for a propellant system consisting of (i) a liquefied HFA propellant, (ii) a co-solvent, and (iii) 0-5% w/w water.

The remaining claims are rejected as depending from a rejected claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 8-9 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claims 8-9 are internally inconsistent, because parent claim 1 has been amended to claim a "pharmaceutical aerosol formulation…which **consists of** (i) salmeterol, a stereoisomer thereof, or a physiologically acceptable salt thereof in solution and (ii) a propellant system…" The use of closed, "consists of," claim language in parent claim 1 and open, "contains," claim language in dependent claims 8-9 to describe the overall formulation is not mutually compatible. Similarly, claim 13 is internally inconsistent, because its parent claim, claim 1, utilizes "consists of" language to describe the overall formulation claimed whereas dependent claim 13 utilizes "contains" language. Appropriate correction is required.

Claim 16 is internally inconsistent with parent claim 1, because the formulation of claim 1 is limited to formulations consisting of (i) salmeterol, a stereoisomer thereof, or a physiologically acceptable salt thereof in solution and (ii) a propellant system comprising a liquefied HFA propellant, a co-solvent, and 0-5% w/w water" and step (a) of claim 16 is generic to any active agent. Similarly, the claimed pharmaceutical formulation is limited to "a co-solvent;" thus, the inclusion of one or more co-solvents in step (b) of claim 16 is inconsistent with claim 1.

The remaining claims are rejected as depending from a rejected claim.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1-3, 6-7, 12-14, and 18-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-8 of U.S. Patent No. 7,347,199 (USPN '199) in view of McNamara et al. (U.S. Patent No. 6,423,298).**

It is noted that both sets of claims claim formulations or pressurized metered dose inhalers (pMDIs) containing formulations comprising dissolved salmeterol, a hydrofluorocarbon propellant (e.g. HFA 227, HFA 134a, or mixtures thereof), cosolvent (e.g. ethanol or polyethylene glycol). The primary difference between the claims of the instant application and the claims of USPN '199 is that the claims of USPN '199 do not recite the limitation that the compositions contain water in an amount of 0-5% w/w or added acid. The deficiency regarding the amount of water is prima facie obvious, because the claims of USPN '199 do not indicate that water has been added. Thus, the claims of USPN '199 necessarily comprise 0% w/w water and are an obvious variant of the claims of the instant application. It is noted that claim 6 of USPN '199 claims a pMDI wherein the active agent is a beta-adrenergic agonist selected from the group consisting of salbutamol, formoterol, salmeterol, and TA 2005. Thus, it would have been a prima facie obvious modification of the claimed pMDI of USPN '199 to select salmeterol as the active agent.

Regarding the inclusion of acid, McNamara's teachings cure this deficiency. McNamara teaches pharmaceutical solution formulations, wherein in one embodiment stabilizers are added to the formulation, wherein **preferred stabilizers are those which influence pH, such as hydrochloric acid, sulfuric acid, nitric acid, phosphoric acid, ascorbic acid, and citric acid** (col. 3, line 64 through col. 4, line 11). **Stabilizers are used in amounts up to 1,000 ppm, most preferably 20-40 ppm** (col. 4, lines 13-15; claims 8-13). By illustration, assuming a total

formulation mass of 100 grams and that the resulting formulation has a density of about 1 g/mL (i.e. a volume of 100 mL), 1,000 ppm (i.e. 0.1 g of acid), 100 ppm (i.e. 0.01 g of acid), 10 ppm (i.e. 0.001 g of acid), and 1 ppm (i.e. 0.0001 g of acid) of HCl acid added to stabilize the formulation would reasonably correlate to pH values of 1.56, 2.56, 3.56, and 4.56, respectively. McNamara's formulations may comprise salmeterol in solution. Thus, the inclusion of acid to solution formulations of salmeterol is a prima facie obvious modification. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-3, 6-7, 12-14, and 18-21 *prima facie* obvious over claims 1-8 of U.S. Patent No. 7,347,199 (USPN '199) in view of McNamara et al. (U.S. Patent No. 6,423,298).

***Response to Arguments***

Applicant's arguments filed November 17, 2009 have been fully considered but they are not persuasive. Applicants traverse this rejection by noting that McNamara teaches solution formulations comprising two or more active agents, in which one of the active agents is in the form of a solution, and McNamara's silence regarding the inclusion of a proper amount of water renders reliance on McNamara improper.

The Examiner respectfully disagrees. It is conceded that McNamara teaches aerosol formulations comprising one active in solution and a second active in suspension. However, this is considered off point because McNamara is cited to demonstrate that it was known to include mineral acids to stabilize solution formulations of active agents, such as salmeterol. Thus, based on the knowledge gleaned from McNamara that active agents in solution, such as salmeterol, may be stabilized by the addition of mineral acids, an ordinary skilled artisan would have

modified the claims of USPN '199 to include a mineral acid to stabilize the dissolved active agent. The rejection is maintained.

**(1) Claims 1-3, 5-7, 9, 12, and 14-17 remain provisionally rejected as being unpatentable over claims 2-3, 6-7, 11, 19, 22, 24, 28-32, 35-36, 40-47, 50-52 of copending Application No. 10/504,151 (copending '151) in view of Lewis et al. (U.S. Patent No. 6,716,414) ("Lewis"); and (2) claims 1-3, and 5 are provisionally rejected as being unpatentable over claims 14-15 and 25-26 of copending Application No. 11/408,026 (copending '026) in view of McNamara et al. (U.S. Patent No. 6,423,298).**

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are overlapping in scope and mutually obvious. Independent claim 1 of the instant application claims a pharmaceutical aerosol solution formulation comprising salmeterol active agent, HFA propellant, cosolvent, 0-5% w/w water (0% water reads on less than 500-1,500 ppm water), wherein the amount of cosolvent is no more than 35% w/w of the total weight of the formulation. Independent claim 32 of copending '151 claims a standard aluminum container containing a pharmaceutical aerosol solution formulation comprising (1) an active agent selected from formoterol or a stereoisomer, physiologically acceptable salt, and solvate thereof, (2) a liquefied HFA propellant, (3) a co-solvent (i.e. ethanol), (4) less than 1,500 ppm of water based on the total weight of the formulation, and (5) between 1.0% w/w and 20% w/w HCl present in an amount equivalent to between 0.030% and 0.045% w/w of 1M HCl. The cited dependent claims of the instant application and of copending '151 have similar and overlapping co-solvent Markush groups, claimed particle sizes, pH ranges,

additional active agent Markush groups, and the same steps in the claimed methods of preparing pharmaceutical formulations. The other cited dependent claims in both applications also recite the same or substantially similar limitations.

The primary difference between applications is that the claims of copending '151 require that the principal active agent is formoterol, excluding claim 14 of copending '151, the claims of the instant application do not specify the container material, and the claims of the cited copending Applications do not require added mineral acid. This deficiency is cured in part by the teachings of Lewis, which is solely provided to demonstrate that salmeterol, formoterol, and TA 2005 are art recognized as being beta2-agonist bronchodilators (col. 5, lines 30-33 of Lewis), which are expected to exhibit similar bronchodilating effects. McNamara's teachings, set forth above cure the deficiency regarding the presence of added acid in copending '026. Regarding the use of a standard aluminum canister, this would have been prima facie obvious modification, as evidenced by claim 13 of the instant application, which explicitly identifies standard aluminum as a suitable canister material. Therefore, it would have been obvious to substitute one beta2 agonist for another, to use standard aluminum as the canister material, and an ordinary skilled artisan would have had a reasonable expectation that upon substitution the resulting formulation would have similar bronchodilating properties. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-3, 5-7, 9-12, and 14-17 *prima facie* obvious over claims 2-3, 6-7, 11, 19, 22, 24, 28-32, 35-36, 40-47, 50-52 of copending Application No. 10/504,151 (copending '867) in view of Lewis et al. (U.S. Patent No. 6,716,414) ("Lewis"). Similar reasoning was used in the analysis of copending 11/408,026 in view of McNamara et al. (U.S. Patent No. 6,423,298).

This is a provisional obviousness-type double patenting rejection.

***Response to Arguments***

Applicant's arguments filed November 17, 2009 have been fully considered but they are not persuasive. Applicants traverse the above provisional obviousness-type double-patenting rejections over copending Application No. 10/504,151 (copending '867) in view of Lewis et al. (U.S. Patent No. 6,716,414) ("Lewis") and over copending 11/408,026 in view of McNamara et al. (U.S. Patent No. 6,423,298) by reiterating the traversal arguments presented regarding the non-provisional obviousness-type double-patenting rejections over U.S. Patent No. 7,347,199 (USPN '199) in view of McNamara et al. (U.S. Patent No. 6,423,298). The rebuttal of these arguments is herein incorporated by reference. The rejections are maintained.

***Conclusion***

**Claims 1-9 and 12-17 are rejected. Claims 18-22 are withdrawn by original presentation. No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, ~10:00-6:00 and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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